

## ABSTRACT

Formulations for controlled, prolonged release of bioactive molecules such as therapeutic proteins, peptides and oligonucleotides have been developed. These  
5 formulations are based on solid microparticles or nanoparticles formed of the combination of biodegradable, synthetic polymers such as poly (lactic acid) (PLA), poly (glycolic acid) (PGA), and copolymers thereof. Bioactive molecules are coupled to hydrophilic polymers such as polyethylene glycol or polypropylene glycol and formulated to provide controlled release. The bioactive molecules are more stable,  
10 less immunogenic and have improved release rate profiles with lower burst levels and increased drug loading relative to the same bioactive molecules lacking coupled hydrophilic polymers. The controlled release formulations can be administered by injection, by inhalation, nasally, or orally.